

Standardizing the Standards: A Road Map for Establishing, Implementing and Unifying Standards in Your Organization

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ABSTRACT

Electronic data submission is the future of clinical trials and reviewers will soon have the statutory authority to reject submissions that do not conform to expectations (e.g., via PDUFA V, section XII in the US). Data standards comprise the core of these expectations with the Standard Data Tabulation model (SDTM) standards as the centerpiece. The extensive body of existing guidance is undergoing rapid development and expansion, including the addition of therapeutic area standards which supplement and extend the existing SDTM implementation guidance. As the deadline for standardized submissions approaches, it is incumbent upon all organizations involved in the pharmaceutical industry to internalize the standardization of data collection, transformation, and analysis to ensure compliance with emerging regulatory requirements.

This paper explores the challenges of developing, implementing, and maintaining organizational SDTM standards that are flexible, current and harmonized with industry standards. We illustrate how a standards initiative can be established and managed, highlighting the fundamental need for organizational commitment, the value added by SDTM and functional area subject matter experts, and the importance of an extensible infrastructure that provides process and content support to study teams. This infrastructure encompasses standard CRFs, comprehensive mapping specifications, programming tools, and an extensive professionalization of standards knowledge including in-depth training and standards implementation support for study teams. We will discuss this initiative, outlining the challenges and opportunities along with providing a roadmap for ongoing development activities to maintain currency, while extending and embedding the role of standards in the organization.

INTRODUCTION

The pharmaceutical and biotech industry must navigate a landscape of strict regulations and ever-changing standards and as knowledge workers in this industry, we must conform to these standards to ultimately satisfy the demands of our stakeholders, be they regulatory agencies, shareholders and/or sponsors. As successful businesses, we must leverage these standards to our advantage, utilizing them to enable greater efficiencies and improving our financial performance. To achieve these vital goals, we must identify, adapt to, and implement applicable standards, effectively train our staff and provide them with quality tools to efficiently implement these standards, and maintain the currency of our application of standards, while harnessing our technical expertise to achieve superior quality results.

The key to this challenge is to design and implement a robust infrastructure that facilitates organizational learning in the face of a continuous evolution of standards. In this paper, we present a roadmap for developing and implementing organizational SDTM data transformation standards. At the center of this initiative is a knowledge management system that can steer the organization toward a robust, flexible infrastructure facilitating adaptation to changing standards and tools enabling project teams to efficiently achieve a high quality, uniform SDTM implementation. However, any system must rely on human resources for implementation and evolution so we place a heavy emphasis on the importance of an operational workforce comprised of subject matter and technical experts who can train and support individual contributors to become standards professionals.

The core focus among regulatory agencies is data standardization through the SDTM. Inherent in the concept of standards is the tenet that they are applied uniformly. This means that all SDTM submissions produced by an organization should present a consistent interpretation and application of published standards. While there are ample resources for guiding SDTM data transformations (e.g., *Study Data Tabulation Model Implementation Guide: Human Clinical Trials V3.1.2* (CDISC, 2008); *Amendment 1 to the Study Data Tabulation Model (SDTM v1.2 and the SDTM Implementation Guide: Human Clinical Trials V3.1.2* (CDISC, 2011)) there is still substantial room for interpretation on how these standards should be applied to any given study. This ambiguity on the application of the standards can often result in different, though equally defensible interpretations of how certain data should be transformed. Thus, to bring uniformity across an organization's SDTM data transformation work, organizational standards that support and extend the industry guidance are critical to ensure a uniform approach to all SDTM data transformations produced by an organization. Benefits of such uniformity include efficiencies in training and task completion and quality assurance

because organizational standards are developed by subject matter experts. Further, organizational standards also enable an organization to quickly adapt to changing industry standards by providing common tools and work processes to update organizational standards as the industry evolves.

As Rozwell, Kush, Helton, Newby & Mason (2009) note, clinical studies are greatly facilitated by the application of data standards, and, if implemented from the beginning, can result in significant time and cost savings over the life of the study (i.e., savings of 40% to 90% on various aspects of a study are possible). However, if the standards are initiated only on the back end to bring the data in line with SDTM standards for the purpose of meeting regulatory demands, there is likely to be a net cost to the application of standards. Indeed, Abolafia (2012) acknowledges this phenomenon, noting many sponsors find implementing SDTM to result in additional cost because they are focused too much on the end product – SDTM compliant data sets for submission to the Food and Drug Administration (FDA). In fact, he argues the focus should shift to the beginning of a study's conceptualization and emphasize data standards throughout the study's life cycle in order to realize the greatest return on investment by "collecting standardized data instead of standardizing collected data" (Abolafia, 2012, n.p.). To address this issue, many sponsors and CROs have established their own internal standards that guide the full range of study tasks to conform to SDTM standards resulting in shortened durations in all phases of data handling, efficient work flows, quicker ramp-up of new staff, and easier incorporation of additions or changes to industry standards (Dubman, Hinkson, Soloff, Fritsche, & Tandon, 2011).

This paper presents a roadmap for the establishment of a full range of organizational standards designed to accurately, uniformly and efficiently support the implementation of SDTM data standards at each step of the study lifecycle. Since these standards are continuously under review, revision, and extension (e.g., the FDA has a roadmap in place to publish fifty-eight therapeutic area (TA) standards by 2017 (FDA, 2012)), a key aspect of this initiative is the need to quickly and efficiently identify and integrate changes and additions to these industry standards into the organizational standards while disseminating these changes to study teams for integration in project work as appropriate. As Steffens (2012) notes, "standards change, they are meant to change, what we need to work on is the infrastructure/technology that easily adapts to changes without re-inventing the wheel" (n.p.). It is tempting to think of an organizational standards initiative as the creation of tools that will speed up our typical work. Rather, what we should be doing is conceiving of a process to consume industry standards information, transform it into actionable information, and then apply that information in our work processes. At its core, we describe a knowledge management effort instead of a tool development endeavor that is designed to facilitate the management of knowledge as it evolves, enabling the transmission of this knowledge efficiently through the organization until it is reflected in our products. Such an effort is focused on developing a flexible, adaptable infrastructure with extensible modules that can be reused and/or repurposed as standards change. Following this theme of recycling, the initiative also leverages the experience and lessons learned from other technology and knowledge management initiatives to create a process that can rapidly utilize information about problems or gaps in the standards application tools or training to produce updates and solutions better targeted to the needs of study teams.

BACKGROUND

As Drucker (1988) asserts, knowledge is the key to sustaining an organization's competitive advantage and economic success. Yet, gaining a firm grasp on this concept often proves elusive since there are so many different ways to conceptualize what is meant by knowledge, and further, how we can exploit our knowledge for business gain. To fill this gap, the field of knowledge management has emerged which seeks to frame how organizations create, maintain, store, disseminate, and leverage knowledge to improve organizational efficiency and effectiveness (Easterby-Smith & Lyles, 2011; Fuller, 2012; Nonaka, 2005). However, unlike physical assets, an organization's knowledge is intangible and is inextricably linked to its human resources whose experience, perceptions and judgment filter the information and in doing so transform the explicit knowledge into a much richer tacit knowledge base capable of enabling the organization to leverage its considerable explicit knowledge for business advantage (Fahey & Prusak, 1998). Data and/or information is often seen as a static unit that can be captured, stored and retrieved as needed, often through some technological means such as a database. Knowledge, on the other hand, can be conceptualized as a flow of data or information, which is constantly being generated and adapted by individuals as they go about their work. While information and data can be contained in information management systems, the application of this data is inextricably linked to the individuals using the data (Fahey & Prusak, 1998). Thus, it is critical that in facilitating the application of data and information for business purposes, i.e., knowledge management, a strong emphasis is placed on the individuals who must apply the information in their work responsibilities.

By conceptualizing knowledge management in this way, the challenges of knowledge management become clear: we must move information, apply it to new settings, retain it within the organization and transmit it to new knowledge workers in the organization (Spender, 2009). Specifically as it applies to the clinical trial industry, there are numerous organizations that are generating vast amounts of data standards information in support of regulatory requirements for standardized submissions of pharmaceutical data (e.g., CFAST, CDISC, CDER, CBER, NCI Vocabulary services, etc.). It is imperative that organizations responsible for applying these standards to their submissions develop and

implement a comprehensive knowledge management system that facilitates the capture and flow of information through their organization. Any such endeavor must enable the internalization of standards into meaningful information that can be transmitted to all who need it in a timely and effective manner. Further, study teams must be adequately trained to use and apply the standards in an appropriate, uniform, and efficient manner to conform to ever-evolving regulatory expectations. As standards change, the organization must be capable of recognizing these changes, swiftly incorporating them into their organizational knowledge and applying them as appropriate in their products.

DISCUSSION

The universe of data standards supporting SDTM is rapidly evolving and expanding to encompass all aspects of study design, conduct and submission. Figure 1 presents a graphical representation of the universe of foundational standards for the clinical research process (CDISC, 2013a). While there are numerous functional standards that cover the whole lifecycle of a clinical trial, beginning with Protocol and Study design through statistical analysis standards (i.e., ADaM), the central focus of this initiative is centered on SDTM standards which implicitly involve standardization of certain upstream tasks in data collection while driving the analysis of the collected data. Currently, sponsors are strongly encouraged to utilize SDTM standards, though, estimated in 2016, the FDA will have the authority to require conformance to SDTM standards for all investigational new drug (IND) submissions (Food and Drug Administration, 2013). As such, the focus of this initiative is primarily on the SDTM and the impact its requirements have on the design and content of its immediate antecedents (e.g., CRF, EDC database design).

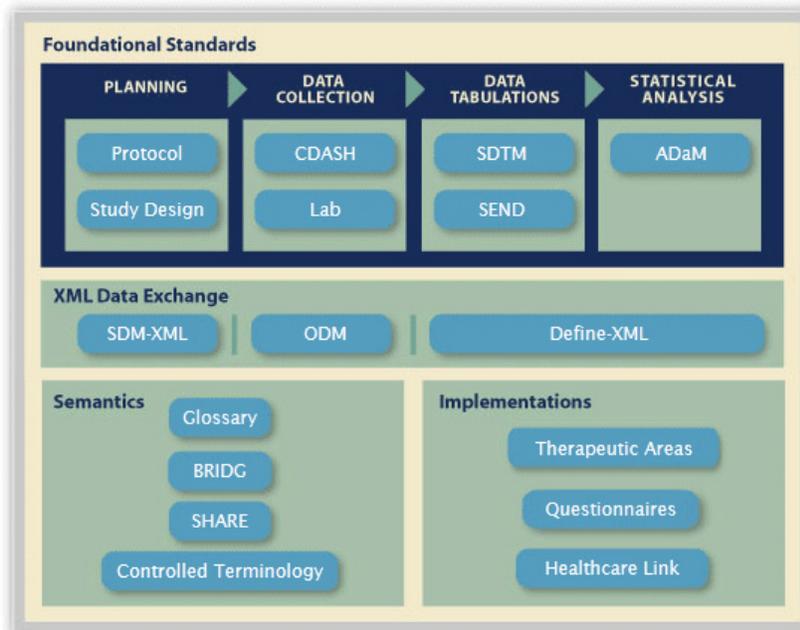


Figure 1. CDISC Foundational Standards

As noted by Rozwell, et al. (2009) and Abolafia (2012), the greatest return on investment is gained through the application of standards early in the study planning process and throughout the lifecycle of a clinical trial. Looking to maximize the gain from the use of industry standards, this organizational initiative is intended to develop a comprehensive library of standard data elements, tools, and utilities to support faster, more uniform clinical trial execution that conforms to industry standards and enables the organization to realize significant efficiencies. This initiative leverages both explicit and tacit knowledge integrated in a robust system designed to be easily adaptable as industry standards evolve; i.e., the crafting of a learning organization that can build on existing knowledge and grow as the regulatory and industry environment changes. Three key contextual factors form the foundation of the initiative: organizational commitment, resource support, and subject matter experts (SMEs).

CONTEXTUAL FACTORS

Any organizational initiative must have sufficient executive commitment to ensure success (Hoffman & Hegarty, 1993). Commonly, initiative champions emerge among the top management and through their advocacy, support and commitment, organizational change takes root and flourishes throughout an organization (Kulkarni, Ravindran & Freeze, 2006/2007). This initiative has enjoyed strong support from top management both for internal development

and implementation, but also through organizational involvement in industry workgroups, conferences, and Clinical Data Interchange Standards Consortium (CDISC) sponsorship.

Emerging from this strong organizational commitment is a substantial pledge of resources in support of the initiative. Without sufficient human, technology, or monetary resources, no initiative can succeed. This organizational effort has benefitted from substantial release time among key contributors to focus on the development of organizational standards. In addition, top management has encouraged active engagement in the international data standards community by providing funds in support of collaboration with thought leaders in the area of data standards as well as involvement by key individuals in numerous conferences and advisory boards. With substantial return on investment expected from the application of standards from study conception through submission, this investment of resources will result in a net profit for the organization over the long term.

Of primary importance to achieving this vision is the investment in a core group of SDTM subject matter experts from different functional groups whose primary responsibility is to develop, disseminate and maintain the organizational standards and supporting tools and utilities. Central to this activity is collaboratively developing consensus on the organizational interpretation of available industry standards. It is this group of SMEs who are charged with shepherding the consolidation of explicit information and tacit knowledge to achieve a knowledge management system that enables uniform application of data standards across all clinical trial projects.

ORGANIZATIONAL STANDARDS DEVELOPMENT

While all organizations must assess their internal needs, the business environment in which they operate and the existing knowledge base within their organization, this framework highlights what the authors believe are common elements to the development and implementation of organizational standards. This task can be broken into five content or process domains:

1. Industry standards (i.e., SDTM, CDASH, ADaM, therapeutic area, questionnaire guidance, controlled terminology, etc.)
2. Organizational guidance for application of industry standards
3. Dissemination of organizational standards
4. Usage support for organizational standards
5. Review and revision of organizational standards

It is important to note that these five domains interrelate and that at any point, feedback from one domain can initiate changes in others. Figure 2 presents a visual representation of the relationships between these elements.

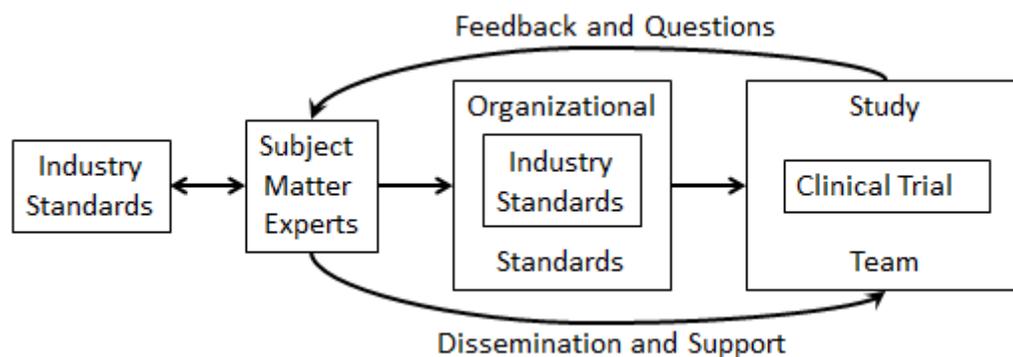


Figure 2. Organizational Standards Work Flow

For CRO's, there can sometimes be an additional layer of sponsor standards that study teams must also incorporate in their work process. In such a case, sponsor standards must take precedent, though the CRO's own organizational standards and industry standards often will still play a role as supplemental guidance in ambiguous situations or as a source for suggested approaches if the sponsor invites the CRO to offer input in how to structure the work.

Industry Standards

The Clinical Data Interchange Standards Consortium was formed in 1997 as a voluntary organization and became an independent, non-profit in 2000. CDISC is an open, multidisciplinary organization whose mission is "to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare" (2013b). The CDISC suite of standards supports medical research of any type from protocol development through analysis and reporting of results and enables the harmonization of clinical data according to a common structure with accompanying guidelines for content.

Within three years, regulatory reviewers will have the statutory authority to reject submissions that do not conform to expectations (e.g., via Prescription Drug User Fee Act V (PDUFA V), section XII). Data standards comprise the core of these expectations with SDTM standards as the centerpiece. The extensive body of existing guidance is undergoing rapid development and expansion, including the addition of therapeutic area standards, an effort driven by CFAST (Coalition for Accelerating Standards and Therapies), which supplement and extend the existing SDTM implementation guidance. CFAST is a joint initiative between CDISC, the Critical Path Institute (C-Path), the FDA, and TransCelerate, a charter group of ten leading biopharmaceutical companies formed to accelerate the development of therapeutic area data standards. In support of the FDA's commitments under the Prescription Drug User Fee Act V (PDUFA V) CFAST is charged with coordinating the development of standards for the 58 targeted therapeutic areas by 2017.

As is evident from Figure 1, there are numerous sources which contribute to these standards and because they are designed to be comprehensive and flexible enough to accommodate all manner of medical research, there are aspects of the standards that are open to interpretation in any given situation. Further, the scope and breadth of the available standards coupled with the magnitude of the information to be processed can result in differential application of industry standards across individual projects and between study teams. Complicating matters further, there are multiple versions of SDTM implementation guidance available for use by study teams. Currently, the FDA is accepting version 3.1.2 but version 3.1.3 has been released and will become the accepted version in due time.

The magnitude of the standards information available for use is such that a centralized effort by SMEs to pull together relevant standards information, digest it, and apply it to organizational training, tools and utilities is imperative. No organization can expect a uniform application of available standards to any given clinical trial without a common set of organizationally-endorsed standards application guidelines. The development of organizational standards is designed to harmonize the application of industry standards across multiple implementations of SDTM to ensure consistency and accuracy in data transformations and to ensure the standards used reflect the proper version as required by the FDA and/or the trial sponsor. In addition, the experience of utilizing the standards in a variety of clinical trial projects gives SMEs unique insight into how the industry standards accommodate the requirements of data reporting and review. It is imperative that the SMEs then interact externally in the various working groups and industry organizations to offer feedback and contribute to the evolution of the industry standards.

Organizational Guidance for Application of Industry Standards

To realize the greatest return on investment from implementation of organizational standards, it is critical to integrate standard elements at all phases of the study that are oriented toward achieving conformance of the final submission components to the standards expected by the regulatory agencies (Rozwell, et al., 2009; Abolafia, 2012). To this end, we have developed a library of standards-based components such as protocol and statistical analysis plan (SAP) elements, case report form (CRF) pages in safety domains and accompanying database modules that implement industry standards according to our organizational implementation standards. As a CRO, we recognize all sponsors are different and to this end, we have designed several different options for each standard CRF domain that reflect different common approaches to data collection in each domain (e.g., options to collect times along with dates, page variants that address differential global privacy regulations such as collection of date of birth; options to capture unblinding information, vital signs collection position, linkage between adverse events and concomitant medications, etc.). The standard structure, variable names, and in many cases, controlled terminology impact all downstream functions such as database modules, automated edit checks, data cleaning listings, and SDTM mapping programs and validations. Standardization of these elements facilitate the development of many standard aspects of the clinical study report components including common table, listing, and figure shell options with accompanying programs and validations. The use of organizational standards offers a decided advantage in efficient execution by exploiting the systematic structure of SDTM to reduce variance in the conduct of clinical trials and realize significant operational efficiencies.

As this initiative matures, additional organizational standards for efficacy domains appropriate for common indications will be developed, incorporating the emerging therapeutic area guidance if relevant. Efficacy domains are necessarily more tailored to the particular study; however organizational and industry standards can still be applied. In different therapeutic areas, there are common/typical data collection requirements such as tumor identification and lesion measurements in oncology studies, the Columbia Suicidality Severity Rating Scale instrument which is used for trials in virtually all psychiatric indications among many others, etc. In such cases, CRF, database, and organizational

SDTM mapping standards can be developed since the content and structure is so typical across studies. With time, an exceptionally robust library of common data elements will be developed that can be used as needed to bring organizational standards to a wide array of customized trial designs by applying the necessary standard modules.

CDISC SDTM standards are systematic and follow established patterns across multiple domains. By focusing first on standard safety SDTM domains, the process of developing organizational implementation standards for the different general observation classes can be outlined. The systematicity of the SDTM domain classes can then be leveraged by repurposing both the process and the common data elements to facilitate efficient adaptation of completed work to additional domains and therapeutic areas. Building on the initial success in the core safety data domains, the initiative can extend the library of SDTM components to encompass all SDTM domains defined by CDISC. In addition, therapeutic area standards, which are supplemental guidance for preparing the SDTM domains for specific therapeutic areas must become part of the organizational standard as they are released by CFAST and their coalition partners. Because industry standards are ever-evolving, in order for organizational standards to remain relevant and continue to support superior performance, it is vital to establish sustainable, reusable data elements and development processes that can continuously adapt to changes in the industry. Sufficient investment must therefore be made to ensure the initial investment is sustained and the currency of the enterprise is protected.

Dissemination of Organizational Standards

Since CDISC SDTM data standards are estimated to be required of all submissions beginning in 2016, it is incumbent that all study teams be prepared to implement these standards in a consistent and efficient manner. Thus, the foundation for success must be the professionalization of SDTM and related standards knowledge among functional groups involved in study planning, data collection, data transformation, and statistical analysis. At each point in a study's lifecycle, functional group representatives with a sound understanding of standards must work to ensure the study's conformance. Organizational standards assist study teams in this by providing interpretation and application guidance for frequently encountered scenarios and common database structures. It is vital that a core group of standards specialists receive the education necessary to engage in an intense manner with the industry and organizational standards and to apply the tenets and philosophies of these standards to new and complex study designs. SMEs are responsible for designing and disseminating this in-depth education to standards specialists who are, in turn, responsible for SDTM mapping specifications and consultation on CRF design. In addition, SMEs develop and deliver training on supportive tools and utilities that enable efficient application of standards and contribute to organization-wide communications such as monthly newsletters and broadcast emails that inform study teams of updates to industry and organizational standards.

Since a basic understanding of industry and organizational standards is vital for all functional units involved in clinical trial design and execution, it is important that role-appropriate CDISC expertise be a common goal in annual performance reviews to ensure project teams are prepared to meet the upcoming regulatory demands and can effectively implement data standards in study work. In support of such requirements, role-based standards training and reference materials, developed by SMEs, should be readily available and fully integrated into the career development plans of all involved in data-oriented study work with this instruction documented in individual training records.

Usage support for Organizational Standards

Industry standards are complex and at times, ambiguous enough that organizational guidance for implementation is critical for consistent application of the standards. The complexity and scope of all data sources that must be brought to bear for standards implementation on a clinical trial is substantial. Applying these standards to any given study is a challenging task and it is critical that adequate support from subject matter experts be readily available to all study teams. To address this need, this initiative utilizes multimodal channels of feedback to support study teams in their implementation of SDTM standards.

A SDTM implementation wiki that addresses both industry standards principles along with organization-specific implementation guidance is available on the intranet for reference by all study teams. The content for this wiki was created by and is maintained by SMEs who are charged with continually updating the site as needed to ensure accuracy and currency of the information. SMEs also provide on-call support to all study teams on interpretation and application of standards and study-specific data handling issues that impact SDTM implementation. Thus, through documentation, consultation with SMEs, and ongoing training on organizational and industry standards, employees have a wealth of information available to them designed to facilitate an accurate, uniform application of SDTM standards in all phases of a study's lifecycle.

Sustainability of Organizational Standards

The ever-changing nature of the industry and the ongoing maturation of data standards necessitate the continuous maintenance of corresponding organizational standards. Such an endeavor is vital if the initial investment of resources is to remain viable over time. To this end, sustainability of organizational standards involves both external and internal factors.

To ensure organizational standards reflect the latest in industry guidance, it is imperative that SMEs remain engaged with external standards groups such as CDISC, CFAST, NCI, CDER, and CBER, among others. Environmental scanning is the process of utilizing information about external organizational forces for strategic planning and action (Aguilar, 1967) and SMEs must effectively identify changes and emerging trends in the industry standards and translate these updates into actionable changes to the organizational standards to ensure they are up-to-date. By staying current on the happenings within the industry, SMEs can ascertain how new versions of standards, emerging initiatives, or updates to regulatory expectations can be integrated into the internal organizational standards and work with study teams to disseminate the updates and ensure that the company's products reflect the latest thinking on standards application and the expectations of reviewers. For CROs this is particularly important since often, sponsors look to CROs as authorities on reviewers' expectations. It is therefore squarely within a CROs mandate to ensure they are well versed on the latest details of industry data standards and can nimbly apply these details to their work for sponsors.

Continuity of organizational knowledge is paramount if organizational standards are to remain a viable source of business intelligence and operational advantage. Human resources are often a shifting landscape, and retention of key SMEs and other experienced project leaders is not always possible. Therefore it is important to keep an eye toward continuity among SMEs and key resources involved heavily in directing SDTM work (Bangerter, 2002). There is a considerable degree of experience and judgment necessary for the accurate application of SDTM standards to trial data. Thus, it is important to plan for continuity by routine incorporation of junior resources to facilitate norming of these junior SMEs to the organizational standards development process and integrating them into the collective knowledge base (Levine & Moreland, 1999).

As the organizational standards are utilized to interpret and apply the industry standards to a wide range of clinical trial databases, subtle implications and variances may emerge that inform the development and revision of industry standards. In addition, as the push for greater detail and revision of industry standards increases along with the development of therapeutic area guidance, it is incumbent that SMEs interact with the larger standards community to offer insight and feedback and to collaborate with standards working groups as appropriate to ensure the industry data standards evolve to fully and efficiently support all manner of clinical trial research. Indeed, this effort is a collaboration of government, industry, and not-for-profits to bring improved therapeutic agents to market efficiently to meet the needs and demands of patients.

IMPLICATIONS FOR PRACTICE

The industry is inexorably moving toward required adaptation of common standards for data structure and, through controlled terminology, content. It is incumbent upon all involved in clinical trial work to embrace this growing body of industry standards and ensure uniform implementation for each submission to regulatory agencies. This paper has presented a roadmap for developing and implementing organizational standards that support industry standards based on CDISC's SDTM. This effort is conceived of as a knowledge management initiative rather than as the creation of a static library of standard documentation. That the application of data standards requires judgment, experience, and customization to accurately apply to any given clinical trial brings this effort into the realm of tacit knowledge and involves a more nuanced, process-oriented approach that emphasizes how we as an organization interpret and apply industry standards.

By emphasizing the dynamic, evolving nature of data standards and building a continuous review process to ensure organizational standards remain current and aligned with the latest industry standards, an organization can ensure ongoing compliance with the latest guidelines. Of paramount importance is the systematic quality of SDTM which also applies to the development process. Once an organization has in place a process for applying industry standards in their preferred way, tailored to their standard approach to data collection and transformation, that process can easily and efficiently be replicated for all domains and general observational class of data. This systematicity also facilitates the potential for substantial operational efficiencies since all functional groups become so familiar with the content and structure of the general classes of domains. This familiarity leads to reduced time to completion of each step in a trial's lifecycle and improved quality since organizational standards support greater accuracy and uniformity in the application of industry standards.

While this paper has centered on the impending requirement from the FDA for use of SDTM in all submissions, it is important to note that the pharmaceutical industry is a global industry and there are a number of other regulatory agencies who will no doubt be moving toward mandatory data standards if they have not already begun the effort. The roadmap presented herein highlights the key concepts of organizational support, systematicity and reusability of standard components, and sustainability of the organizational standards develop process. Whether other agencies adopt CDISC SDTM or forge their own interpretation of data standards, these principles should guide organizations in adapting and extending their organizational standards to address the particular needs of the various regulatory agencies.

Organizational standards have clear applications for all organizations involved in preparing submissions, be they

CROs, large pharmaceutical companies or small start-up companies looking for their first approval. Obviously, CROs benefit greatly by streamlining their operations and improving efficiencies and uniformity of implementation across all projects regardless of sponsor. As an added benefit, CROs can leverage their work with multiple sponsors to bring to bear their knowledge base of sponsor-specific requests, preferences, and standards to develop a library of standards tailored to enabling further customization to the individual client's particular needs and requirements.

Indeed, many large, established pharmaceutical companies have standards committees that generate their own take on SDTM standards implementation. Whether they perform their own data transformations or whether they contract this work to CROs, their organizational standards provide the primary guidance in structuring the data transformations in preparation for submission. It is important to note that as we approach the point where SDTM will be the required standard for submission to the FDA, it is imperative these companies recognize the evolving nature of the standards and have a knowledge management system in place to cope with the upcoming therapeutic area standards and the evolving requirements of the standard SDTM domains.

For those companies that do not operate with organizational standards as an overlay to the industry standards, we argue this is a vital need that can improve either their own data collection, management and transformation work, or, if they contract with CROs for these tasks, these standards can ensure the vendor applies the standards in ways acceptable to the sponsor. However, if the sponsor is not in a position to provide organizational standards, they should confirm that their CRO of choice has expertise with industry standards and can employ a robust data management system able to facilitate the application of current industry standards with accuracy and efficiency throughout the entire lifecycle of a study.

In the dynamic and detail-intensive domain of data standards it is imperative that organizations, be they CRO or pharma, recognize that the landscape of operation will be undergoing a significant shift once regulatory agencies mandate data standards for all submissions. We argue that organizational standards, crafted by SMEs, provide a valuable interpretive layer that facilitates high quality, accurate, and efficient implementation of industry standards. The magnitude of this information, coupled with the judgment and experience necessary to appropriately apply the standards argue for a knowledge management approach to maintaining and applying these standards by emphasizing reusable, systematic processes and common elements that can be repurposed or modified as the industry standards evolve. This knowledge-management approach invites all organizations to pick their method for application of standards based on their own infrastructure and expertise in therapeutic areas, while empowering their study teams to be true stakeholders in continuous improvement.

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